Coronavirus disease 2019: the harms of exaggerated information and non-evidence-based measures

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The evolving coronavirus disease 2019 (COVID-19) pandemic[1] is certainly cause for concern. Proper communication and optimal decision-making is an ongoing challenge, as data evolve. The challenge is compounded, however, by exaggerated information. This can lead to inappropriate actions. It is important to differentiate promptly the true epidemic from an epidemic of false claims and potentially harmful actions.

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Problems with early estimates and responses to the COVID-19 epidemic

- A highly flawed non-peer-reviewed preprint claiming similarity with HIV-1 drew tremendous attention; it was withdrawn, but conspiracy theories about the new virus became entrenched
- Even major peer-reviewed journals have already published wrong, sensationalist items
- Early estimates of the projected proportion of global population that will be infected seem markedly exaggerated
- Early estimates of case fatality rate may be markedly exaggerated
- The proportion of undetected infections is unknown but probably varies across countries and may be very large overall
- Reported epidemic curves are largely affected by the change in availability of test kits and the willingness to test for the virus over time
- Of the multiple measures adopted, few have strong evidence, and many may have obvious harms
- Panic shopping of masks and protective gear and excess hospital admissions may be highly detrimental to health systems without offering any concomitant benefit
- Extreme measures such as lockdowns may have major impact on social life and the economy; estimates of this impact are entirely speculative
- Comparisons with and extrapolations from the 1918 influenza pandemic are precarious, if not outright misleading and harmful

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Fake news and withdrawn papers: Based on Altmetric scores, the most discussed and most visible scientific paper across all 20+ million papers published in the last 8 years across all science is a preprint claiming that the new coronavirus' spike protein bears "uncanny similarity" with HIV-1 proteins.[2] The Altmetric score of this work has reached an astronomical level of 13725 points as of March 5, 2020. The paper was rapidly criticized as highly flawed and the authors withdrew it within days. Regardless, major harm was already done. The preprint fueled conspiracy theories of scientists manufacturing dangerous viruses and offered ammunition to vaccine deniers. Refutation will probably not stop dispersion of weird inferences.

The first report documenting transmission by an asymptomatic individual was published in the *New England Journal of Medicine* on January 30. However, the specific patient did have symptoms, but researchers had not asked.[3] Understanding the chances of transmission during the asymptomatic phase has major implications for what protective measures might work.

Lancet published on February 24 an account from two Chinese nurses of their front-line experience fighting coronavirus. The authors soon retracted the paper admitting it was not a first-hand account.

These examples show how sensationalism affects even top scientific venues. Moreover, peer-review may malfunction when there is little evidence and strong opinions. Opinion-based peer-review may even solidify a literature of spurious statements. As outlined below, for the main features of the epidemic and the response to it, circulating estimates are often exaggerated, even when they come from otherwise excellent scientists.

Exaggerated pandemic estimates: An early speculation that 40-70% of the global population will be infected went viral.[4] Early estimates of the basic reproduction number (how many people get infected by each infected person) have varied widely, from 1.3 to 6.5.[5] These

estimates translate into many-fold difference in the proportion of the population eventually infected and dramatically different expectations on what containment measures (or even any future vaccine) can achieve. The fact that containment measures do seem to work, means that the basic reproduction number is probably in the lower bound of the 1.3-6.5 range, and can decrease below 1 with proper measures. The originator of the "40-70% of the population" estimate tweeted on March 3 a revised estimate of "20-60% of adults", but this is probably still substantially exaggerated. Even after the 40-70% quote was revised downward, it still remained quoted in viral interviews.[6]

Exaggerated case fatality rate (CFR): Early reported CFR figures also seem exaggerated. The most widely quoted CFR has been 3.4%, reported by WHO dividing the number of deaths by documented cases in early March.[7] This ignores undetected infections and the strong age-dependence of CFR. The most complete data come from Diamond Princess passengers, with CFR=1% observed in an elderly cohort; thus, CFR may be much lower than 1% in the general population; probably higher than seasonal flu (CFR=0.1%), but not much so.

Observed crude CFR in South Korea and in Germany[8], the countries with most extensive testing, is 0.9% and 0.2%, respectively as of March 14 and crude CFR in Scandinavian countries is about 0.1%. Some deaths of infected, seriously ill people will occur later, and these deaths have not been counted yet. However even in these countries many infections probably remain undiagnosed. Therefore, CFR may be even lower rather than higher than these crude estimates.

Exaggerated exponential community spread: At face value, the epidemic curve of new cases outside China since late February is compatible with exponential community spread. However, reading this curve is very difficult. Part of the growth of documented cases could reflect rapid increases in numbers of coronavirus tests performed. The number of tests done

depends on how many test-kits are available and how many patients seek testing. Even if bottlenecks in test availability are eventually removed, the epidemic curve may still reflect primarily population sensitization and willingness for testing rather than true epidemic growth. China data are more compatible with close contact rather than wide community spread being the main mode of transmission.

Extreme measures: Under alarming circumstances, extreme measures of unknown effectiveness are adopted. China initially responded sluggishly, but subsequently locked down entire cities.[9] School closures, cancellation of social events, air travel curtailment and restrictions, entry control measures, and border closure are applied by various countries. Italy adopted country-level lockdown on March 8 and many countries have been following suite.

Evidence is lacking for the most aggressive measures. A systematic review on measures to prevent the spread of respiratory viruses found insufficient evidence for entry port screening and social distancing in reducing epidemic spreading.[10] Plain hygienic measures have the strongest evidence.[10,11] Frequent hand washing and staying at home and avoiding contacts when sick are probably very useful. Their routine endorsement may save many lives. Most lives saved may actually be due to reduced transmission of influenza rather than coronavirus.

Most evidence on protective measures comes from non-randomized studies prone to bias. A systematic review of personal protective measures in reducing pandemic influenza risk found only two randomized trials, one on hand sanitizer and another on facemasks and hand hygiene in household members of people infected with influenza.[11]

Harms from non-evidence based measures: Given the uncertainties, one may opt for abundant caution and implement the most severe containment measures. By this perspective, no opportunity should be missed to gain any benefit, even in absence of evidence or even with mostly negative evidence.

This reasoning ignores possible harms. Impulsive actions can indeed cause major harm. One clear example is the panic shopping which depleted supplies of face masks, escalation of prices and a shortage for medical personnel. Masks, gloves, and gowns are clearly needed for medical personnel; their lack poses health care workers' lives at risk. Conversely, they are meaningless for the uninfected general population. However, a prominent virologist's comment[12] that people should stock surgical masks and wear them around the clock to avoid touching their nose went viral.

Misallocation of resources: Policy-makers feel pressure from opponents who lambast inaction. Also adoption of measures in one institution, jurisdiction, or country creates pressure for taking similar measures elsewhere under fear of being accused of negligence. Moreover, many countries pass legislation that allocates major resources and funding to the coronavirus response. This is justified, but the exact allocation priorities can become irrational.

For example, undoubtedly research on coronavirus vaccines and potential treatments must be accelerated. However, if only part of resources mobilized to implement extreme measures for COVID-19 had been invested towards enhancing influenza vaccination uptake, tens of thousands of influenza deaths might have been averted. Only 1-2% of the population in China is vaccinated against influenza. Even in the USA, despite improvements over time, most adults remain unvaccinated every year.

As another example, enhanced detection of infections and lower hospitalization thresholds may increase demands for hospital beds. For patients without severe symptoms, hospitalizations offer no benefit and may only infect health workers causing shortage of much-needed personnel. Even for severe cases, effectiveness of intensive supportive care is unknown. Excess admissions may strain health care systems and increase mortality from other serious diseases where hospital care is clearly effective.

Lockdowns – for how long? An argument in favor of lockdowns is that postponing the epidemic wave ("flattening the curve") gains time to develop vaccines and reduces strain on the health system. However, vaccines take many months (or years) to develop and test properly. Maintaining lockdowns for many months may have even worse consequences than an epidemic wave that runs an acute course. Focusing on protecting susceptible individuals may be preferable to maintaining country-wide lockdowns long-term.

Economic and social disruption: The potential consequences on the global economy are already tangible. February 22-28 was the worst week for global markets since 2008 and the worse may lie ahead. Moreover, some political decisions may be confounded with alternative motives. Lockdowns weaponized by suppressive regimes can create a precedent for easy adoption in the future. Closure of borders may serve policies focused on limiting immigration. Regardless, even in the strongest economies, disruption of social life, travel, work, and school education may have major adverse consequences.

The eventual cost of such disruption is notoriously difficult to project. A quote of $2.7 trillion[13] is totally speculative. Much depends on the duration of the anomaly. The global economy and society is already getting a major blow from an epidemic that otherwise (as of

March 14) accounts for 0.01% of all 60 million annual global deaths from all causes and that kills almost exclusively people with relatively low life expectancy.

Claims for once-in-a-century pandemic: Leading figures insist that the current situation is a once-in-a-century pandemic.[14] A corollary might be that any reaction to it, no matter how extreme, is justified.

This year's coronavirus outbreak is clearly unprecedented in amount of attention received. Media have capitalized on curiosity, uncertainty and horror. A Google search with "coronavirus" yielded 3,550,000,000 results on March 3 and 9,440,000,000 results on March 14. Conversely, "influenza" attracted 30- to 60-fold less attention although this season it has caused so far about 100-fold more deaths[15] globally than coronavirus.

Different coronaviruses actually infect millions of people every year, and they are common especially in the elderly and in hospitalized patients with respiratory illness in the winter. A serological analysis[16] of CoV 229E and OC43 in 4 adult populations under surveillance for acute respiratory illness during the winters of 1999–2003 (healthy young adults, healthy elderly adults, high-risk adults with underlying cardiopulmonary disease, and a hospitalized group) showed annual infection rates ranging from 2.8% to 26% in prospective cohorts, and prevalence of 3.3%-11.1% in the hospitalized cohort. Case fatality of 8% has been described in outbreaks among nursing home elderly.[17] Leaving the well-known and highly lethal SARS and MERS coronaviruses aside, other coronaviruses probably have infected millions of people and have killed thousands. However, it is only this year that every single case and every single death gets red alert broadcasting in the news.

Comparisons with 1918: Some fear an analogy to the 1918 influenza pandemic that killed 20-40 million people.[18] Retrospective data from that pandemic suggest that early adoption of social distancing measures were associated with lower peak death rates.[19] However, these data are sparse, retrospective, and pathogen-specific. Moreover, total deaths were eventually little affected by early social distancing: people just died several weeks later.[19] Importantly, this year we are dealing with thousands, not tens of millions deaths.

Learning from COVID-19: The Box summarizes the problems with inaccurate and exaggerated information in the case of COVID-19. Even if COVID-19 is not a 1918-recap in infection-related deaths, some coronavirus may match the 1918 pandemic in future seasons. Thus we should learn and be better prepared. Questions about transmission, duration of immunity, effectiveness of different containment and mitigation methods, the role of children in viral spread, and assessment of the effectiveness of vaccines and drugs are essential to settle timely.

This research agenda requires carefully collected, unbiased data to avoid unfounded inferences. Larger-scale diagnostic testing should help get more unbiased estimates of cases, basic reproduction number, and CFR. The research agenda also deserves proper experimental studies. Besides candidate vaccines and drugs, randomized trials should evaluate also the real-world effectiveness of simple measures (e.g. face masks in different settings), least disruptive social distancing measures, and health care management policies for documented cases.

If COVID-19 is indeed the pandemic of the century, we need the most accurate evidence to handle it. Open data sharing of scientific information is a minimum requirement. This should include data on the number and demographics of tested individuals per day in each country. Proper prevalence studies and trials are also indispensable.

If COVID-19 is not as grave as it is depicted, high evidence standards are equally relevant. Exaggeration and over-reaction may seriously damage the reputation of science, public health, media, and policy makers. It may foster disbelief that will jeopardize the prospects of an appropriately strong response if and when a more major pandemic strikes in the future.

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